My dear Luca,

I thought you might like to know that I have obtained a
spontaneously occurring Hfr strain. This appeared in 58-161/F+(Spicer)
under the following peculiar circimstances. I have found that F+,but
not F-,cultures maintained on inspissated egg at 4° tend to die out
slowly over a period of many months. Some weeks ago.I found that
58/Spicer,transduced to F+ and kept on egg as usual,failed to yield
growth when quite large sweeps of growth were transferred to broth.
There was no evidence of lysis or plaque formation. I left the egg
culture on the bench as a reminder to do something about it. About a
week later I noticed that about 20 colonies had grown up on the area
of confluent(but dead) previous growth. Several of these colonies
were normally F+. One of them,however,was Hfr. The recombination
rate is about X 1000 normal; it does not transduce F+ to W677/F-(25
colonies tested & compared with 25 colonies picked from a mixture
with an Nfr culture of the same strain which gave 100% conversion
under the same conditions); 25 Hfr X F- prototrophs appear to be F-
(period of incubation not yet completed). In fact,it seems to behave
exactly as your mustard-induced strain does. The interesting thing
is that UV depresses the fertility of Hfr,a result which I must admit
I anticipated. I have been thinking a lot about Hfr over the last few
weeks and the more I think of it the more it seems to me to fit in
to the view that the F+ agent ix acts as a genetic vector. The theory
now is as follows. F+ is a virus though not necessarily one which
under any circumstances is lytic like a-phage. It is liberated by the
majority(or all)of F+ cells during the early stages of the growth
cycle,and remains adsorbed to the surface of the cell;alternatively,
it is liberated free but is very rapidly adsorbed on to other cells.
When adsorbed by F- cells it is infective but its stability within
a host cell depends on a rather delicate physiological balance so
that,in the case of certain F- populations only a proportion of cells
become infected,F+ being discarded by,or dying in,the remainder. A
small proportion of F+ agents from Nfr strains become intimately assoc-
iated with part of the chromosome(or one of several chromosomes) of the
host cell so that,when these are liberated the chromosome is carried
with them. The effect of UV is to increase the proportion of cells in
which the F+ agent is associated with genetic elements(since UV decreases
F+ transduction at the same time as it increases recombination). In
Hfr strains there has been a mutation of F+ and the establishment of a
new relationship between it and the cell so that all the F+ agents now
become associated with genetic elements; i.e. those F+ agents which,in
Nfr cells,become tied to genetic elements either naturally or as the
result of the new equilibrium induced by UV,can be regarded as phenocop-
ies of the genetic alteration which is Hfr. The Hfr virus,however,is
inherently unstable in F- cells so that it cannot establish itself to
produce Hfr prototrophs. I have been most interested to learn in this
connection that,in Salmonella transduction which appears to be definitely
due to phage carriage the recipient strain may remain phage sensitive
although genetically altered. It is also a fact that only a proportion

of sensitive cells exposed to temperate phage establish a lysogenic relationship with it. I feel that F+ may exist in various "allelic" forms and that its stability within F- cells depends on a very delicate relationship between just the right F+ allele and the right physiological state of the cell. Hence your F+ strain which can be transduced by Waksman F+ but not by K12F+ and with which 50% prototrophs are F-, and my 58/F+ strain which is very poorly transduced to F+ as compared with W677/F+ and with which only 30% prototrophs are F+. I don't know what you think of all this — these are deep waters! I have probably expressed it all very badly. I forgot to mention that my theory as to why Hfr recombination is depressed by UV is that since all the F+ agents are already associated with genetic elements the proportion which do so cannot be increased by UV, while UV depresses the number of vectors which can make effective contact with F- cells. Incidentally my Hfr strain shows a 10-20 fold reduction in recombination rate when crossed with W-677/F+. Unfortunately it is $S^r Az^r$ so I have'nt been able to test the effect of SM on its fertility. Could you send me your Hfr? I tested 20 colonies from a copy of it which I have and all were NfrE+. I was glad to hear of you and your work from Jim. Will you be coming to the S.G.M.Symposium on "Adaptation"? If you do I hope you will stay with us but please let me know as early as you can. Is there no chance of your getting a travel grant to go to Cold Spring Harbor? Both Jim and I think you should be there. With every good wish - *Bill*